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**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
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Sheet 1 of 12

<i>Complete if Known</i>	
Application Number	10/518,003
Filing Date	March 14, 2005
First Named Inventor	Daniel S. MARTIN
Art Unit	1623
Examiner Name	Lawrence E. Crane
Attorney Docket Number	636-C-PCT-US

U. S. PATENT DOCUMENTS

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				
/L.C./	2	WO 02/45720 A1	06-13-2002	SLOAN KETTERING INST. FOR CANCER RES.		

Examiner Signature	/Lawrence Crane/	Date 3/1/2008 Considered
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Translation is attached.
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Sheet 2	of 12	Attorney Docket Number	636-C-PCT-US

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/L.C./	3	PCT International Preliminary Examination Report for SLOAN KETTERING INSTITUTE FOR CANCER RESEARCH, PCT/US01/46886 (Atty. Dkt. #636-A-PCT), "Treatment of cancer by reduction of intracellular energy and pyrimidines," Filed December 4, 2001, Dated July 25, 2003.		
/L.C./	4	Amarante-Mendes, G.P., Finucane, D.M., Martin, S.J., Cotter, T.G., Salvesen, G.S. and Green, D.R., 1998, "Anti-apoptotic oncogenes prevent caspase-dependent and independent commitment for cell death," Cell Death Differ., 5:298-306.		
/L.C./	5	Batova, A., Diccianni, M.B., Omura, Minamisawa, M., Yu, J., Carrera, C.J., Bridgeman, L.J., Kung, F.H., Pullen, J., Amyulon, M.D. and Yu, A.L., 1999, Use of alanosine as a methyladenosine phosphorylase – selective therapy for T-cell acute lymphoblastic leukemia in vitro," Cancer Res., 59:1492-1497.		
/L.C./	6	Berger, N.A., and Berger, S.J., 1986, "Metabolic consequences of DNA damage: The role of poly (ADP-ribose) polymerase as mediator of the suicide response," In: L. Grossman, A.C. Upton, (eds.) Mechanisms of DNA Damage and Repair, pp. 357-363. New York: Plenum Publishing Corporation.		
/L.C./	7	Berns, A., May 2002, "Senescence: A companion in chemotherapy?" Cancer Cell, 309-311.		
/L.C./	8	Bertino, J.R., 1990, "Leucovorin rescue revisited: Editorial," J. Clin. Oncol., 8 (2):193-195.		
/L.C./	9	Bissett, D., Mcleod, H.L., Sheedy, B., Collier, M., Pithavala, Y., Paradiso, L., Pitsiladas, M. and Cassidy, J., 2001, "Phase 1 dose-escalation and pharmacokinetic study of a novel folate analogue A G 2034," Br. J. Cancer, 84:308-312.		
/L.C./	10	Bonfoco, E., Krainc, D., Ankarcrona, M., Nicotera, P. and Lipton, S.A., 1995, "Apoptosis and necrosis: two distinct events induced, respectively, by mild and intense insults with N-methyl-D-aspartate or metric oxide/superoxide in cortical cell cultures," Proc. Natl. Acad. Sci. USA, 92:7162-7166.		
/L.C./	11	Bose, R., Verheij, M., Haimovitz-Friedman, A., Scotto, K., Kucks, Z. and Kolesnick, R., 1995, "Ceramide synthase mediates daunorubicin-induced apoptosis: an alternative mechanism for generating death signals," Cell, 82:405-411.		
/L.C./	12	Boulares, A.H., Yokovlev, A.G., Ivanova, V., Stoica, B.A., Wang, G., Iyer, S. and Smulson, M., 1999, "Role of poly (ADP-ribose) polymerase (PARP) cleavage in apoptosis. Caspase-3 resistant PARP mutant increases rates of apoptosis in transfected cells," J. Biol. Chem., 274:22932-22940.		

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/L.C./	13	Britten, C.D., Rowinsky, E.K., Baker, S.D., Weiss, G.R., Smith, L., Stephenson, J., Rothenberg, M., Smetzer, L., Cramer, J., Collins, W., Von Hoff, D.D., and Eckhardt, S.G., 2000, "A Phase 1 and pharmacokinetic study of the mitochondrial-specific chodacyanine dye analog MKT 011," <i>Clin. Cancer Res.</i> , 6:42-49.			T ²
/L.C./	14	Brondum, J.L. and Moran, R.G., 2002, "Antifolates targeting purine synthesis allow entry of tumor cells into S phase regardless of p53 function," <i>Cancer Res.</i> , 62:5236-5241.			
/L.C./	15	Budihardjo, Ii, Walker, D.L., Svingen, P.A., Buckwalter, C.A., Desnoyers, S., Eckdahl, S., Shah, G.M., Poirier, G.G., Reid, J.M., Ames, M.M., and Kaufmann, S.H., 1998, "6-Aminonicotinamide sensitizes human tumor cell lines to cisplatin," <i>Clinical Cancer Research</i> , 4:117-30.			
/L.C./	16	Cahill, D.P., Kinzler, K.W., Vogelstein, B. and Lengauer, C., 1999, "Genetic instability and Darwinian selection tumors," <i>Trends in Cell Biology</i> , 57-60.			
/L.C./	17	Carson, D.A., Seto, S., Wasson, B., and Carrera, C., 1986, "DNA strand breaks, NAD metabolism, programmed cell death," <i>Exp. Cell. Res.</i> , 164:273-281.			
/L.C./	18	Chatterjee, S., Hirota, H., Belfi, C.A., Berger, S.J. and Berger, N.A., 1997, "Hypersensitivity to DNA cross-linking agents associated with up-regulation of glucose-regulated stress protein GRP 78," <i>Cancer Res.</i> , 57:5112-5116.			
/L.C./	19	Chen, Z.H., Zhang, H. and Savarese, T.M., 1996, "Gene deletion chemoselectivity: codeletion of the genes for p16INK4, methylthioadenosine phosphorylase, and the α - and β -interferons in human pancreatic cell carcinoma lines and its implications for chemotherapy," <i>Cancer Res.</i> , 56:1083-1090.			
/L.C./	20	Constantini, P., Chernyak, B.V., Petronilli, V. and Bernardi, P., 1996, "Modulation of the mitochondrial permeability transition pore by pyridine nucleotides and dithiol oxidation at two separate sites," <i>J. Biol. Chem.</i> , 271:6746-6751.			
/L.C./	21	Cory, A.H., and Cory, J.G., 1994, "Use of nucleoside Kinase deficient mouse leukemia L1210 cell lines to determine metabolic routes of activation of antitumor nucleoside analogs," <i>Adv. Enzyme Regul.</i> , 34:1-12.			
/L.C./	22	Cotter, T.G., Lenon, S.V., Glynn, J.G. and Martin, S.J., 1990, "Cell death via apoptosis and its relationship to growth, development and differentiation of both tumor and normal cells," <i>Anticancer Res.</i> , 10:1153-1160.			

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NON PATENT LITERATURE DOCUMENTS

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/L.C./	23	Dang, C.V. and Semenza, G.L., 1999, "Oncogenic alterations metabolism," Trends Biochem. Sci., 24:68-92.	
/L.C./	24	Dietrich, L.S., Kaplan, L., and Friedland, I.M., 1958, "Pyridine nucleotide metabolism: mechanism of action of the niacin antagonist, 6-aminonicotinamide," J. Biol. Chem. 233:964-968.	
/L.C./	25	Droin, N., Beauchemin, M., Solary, E. and Bertrand, R., 2000, "Identification of a caspase-2 isoform that behaves as endogenous inhibitor of the caspase cascade," Cancer Res., 60:7039-7047.	
/L.C./	26	Eguchi, Y., Shimizu, S., and Tsujimoto, Y., 1997, "Intracellular ATP levels determine cell fate by apoptosis or necrosis," Cancer Res., 57:1835-1840.	
/L.C./	27	Evtodienko, Y.V., Teplova, V.V., Sidosh, S.S., Ichas, F. and Mazal, J.P., 1996, "Microtubule-active drugs suppress the closure of the permeability transition pore in tumor mitochondria," FEBS Lett., 393:86-88.	
/L.C./	28	Fitchen, J.H., Riscoe, M.K., Dana, B.W., Lawrence, H.J. and Ferro, A.J., 1986, "Methylthioadenosine phosphorylase deficiency in human leukemias and solid tumors," Cancer Res., 46:5409-5412.	
/L.C./	29	Formigli, L., Papucci, L., Tani, A., Schivone, N., Tempestine, A., Orlandini, G.E., Capaccioli, S. and Orlandini, S.Z., 2000, "Aponecrosis: Morphological and biochemical exploration of a syncretic process of cell death sharing apoptosis and necrosis," J. Cell Physiol. 182:41-49.	
/L.C./	30	Forrester, H.B., Albright, N., Ling, C.C. and Dewey, W.C., 2000, "Computerized video time-lapse analysis of apoptosis of REC: Myc cells X-radiated in different phases of the cell cycle," Radiat. Res., 154:625-639.	
/L.C./	31	Gaal, J.C., Smith, K.R., and Pearson, C.K., 1987, "Cellular euthanasia mediated by a nuclear enzyme: A central role for nuclear ADP-ribosylation in cellular metabolism," Trends Biochem. Sci., 12:129-130.	
/L.C./	32	Gewirtz, D.A., 1999, "A critical evaluation of mechanisms of action proposed for the antitumor effects of the anthracycline antibiotics adriamycin and daunorubicin," Biochem. Pharm., 57:727-741.	

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/L.C./	34	Green, D.R., 1998, "Apoptotic pathways: The roads to ruin," Cell, 94:695-698.	
/L.C./	35	Grindley, G.B., Lowe, J.K., Divekey, A.Y., and Halaka, M.T., 1976, "Potentiation by guanine nucleosides of the growth-inhibitory effects of adenosine analogues on L1210 and Sarcoma 180 cells in culture," Cancer Res., 36:379-383.	
/L.C./	36	Haimovitz-Friedman, A., Kan, C.C., Ehleiter, D., Persaud, R.S., McLoughlin, M., Fuks, Z. and Kolesnick, R.N., 1994, "Ionizing radiation acts on cellular membranes to generate ceramide and initiate apoptosis," J.Exp. Med., 180:525-535.	
/L.C./	37	Herceg, Z. and Wang, Z.Q., 1999, "Failure of poly (ADP/ribose) polymerase cleavage by caspases leads to induction of necrosis and enhanced apoptosis," Mol. Cell Biol., 19:5124-5133.	
/L.C./	38	Herken, H., Lange, K. and Kolbe, H., 1969, "Brain disorder induced by pharmacological blockage of the pentose phosphate pathway," Biochem. Biophys. Res. Commun., 36:93-100.	
/L.C./	39	Herter, F., Weissman, S.G., Thompson, H.G. et al., 1961, "Clinical experience with 6-aminonicotinamide," Cancer Res. 21:31-37.	
/L.C./	40	Hickman, J.A., 1992, "Apoptosis induced by anticancer drugs," Cancer Metast. Rev., 11:121-139.	
/L.C./	41	Hunting, D., Gowans, B., and Henderson, J.F., 1985, "Effect of 6-AN on cell growth, poly (ADP-ribose) synthesis and nucleotide metabolism," Biochem. Pharmacol., 34:3999-4003.	
/L.C./	42	Janicke, R.V., Sprengart, M.L., Wati, M.R. and Porter, A.G., 1998, "Caspase-3 is required for DNA fragmentation and morphological changes associated with apoptosis," J. Biol. Chem., 273:9357-9360.	

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/L.C./	44	Jones, M., 1980, "Pyrimidine nucleotide biosynthesis in animals: Genes, enzymes and regulation of UMP synthesis," <i>Ann. Rev. Biochem.</i> , 49:253-279.	
/L.C./	45	Kamatani, N., Nelson, Rees, W.A. and Carson, D.A., 1981, "Selective killing of human malignant cell lines deficient in methylthioadenosine phosphorylase, a purine metabolic enzyme," <i>Proc. Natl. Acad. Sci. USA</i> , 78:1219-1223.	
/L.C./	46	Kass, G.E., Eriksson, J.E., Weis, M., Orrenius, S., and Chow, S.C., 1996, "Chromatin condensation during apoptosis requires ATP," <i>Biochem. J.</i> , 318:749-52.	
/L.C./	47	Kerr, J.F.R., Wyllie, A.H., and Currie, A.R., 1972, "Apoptosis: a basic biological phenomenon with wide-ranging implications in tissue kinetics," <i>Brit. J. Cancer</i> , 26:239-257.	
/L.C./	48	King, M.P., and Attardi, G., 1989, "Human cells lacking mtDNA: Repopulation with exogenous mitochondria by complementation," <i>Science</i> , 246:500-503.	
/L.C./	49	King, K.L. and Cidlowski, J.A., 1995, "Cell cycle and apoptosis: Common pathways to life and death," <i>J. Cell Biochem.</i> , 58:175-180.	
/L.C./	50	Ko et al., 2004, "Advanced cancers: eradication in all cases using 3-bromopyruvate therapy to deplete ATP," <i>Biochemical and Biophysical Research Communications</i> , 269:275.	
/L.C./	51	Kroemer, G., 1997, "Mitochondrial implication in apoptosis. Towards an endosymbiont hypothesis of apoptosis evolution," <i>Cell Death Differ.</i> , 4:443-456.	
/L.C./	52	Kroemer, G., Zamzami, N., and Susin, S.A., 1997, "Mitochondrial control of apoptosis," <i>Immunol. Today</i> , 18:44-51.	

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/L.C./	54	Kuida, K., Hayder, T.F., Kuan, C.Y., Gu, Y., Taya, C., Karasuyama, H., Su, M.S.S., Radic, P. and Flavell, R.A., 1998, "Reduced apoptosis and cytochrome c-mediated caspase activation in mice lacking caspase activation in mice lacking caspase 9," <i>Cell</i> , 94:325-337.	
/L.C./	55	Lemasters, J.J., 1999, "Necroptosis and the mitochondrial permeability transition: shared pathways to necrosis and apoptosis," <i>Am. J. Physiol.</i> , 276:G1-6.	
/L.C./	56	Li, H., Zhu, H., Xu, C.J., 1998, "Cleavage of BID by caspase 8 mediates the mitochondrial damage in the Fas pathway of apoptosis," <i>Cell</i> , 94:491-501.	
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/L.C./	60	Marks, D.I., and Fox, R.M., 1991, "DNA damage, poly(ADP-ribosyl)action and apoptotic cell death as a potential common pathway of cytotoxic drug action," <i>Biochem. Pharmacol.</i> 42:1859-1867.	
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				Filing Date	March 14, 2005
				First Named Inventor	Daniel S. MARTIN
				Art Unit	1623
				Examiner Name	Lawrence E. Crane
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/L.C./	63	Martin, D., Matei, C., and Koutcher, J., 2000, "Marked enhancement of radiotherapy-induced tumor regression by an NAD antagonist, 6-aminonicotinamide (6-AN)," Proc. Am. Assoc. Cancer Res., 41:283 (Abstract 1800).		T ²
/L.C./	64	Modica Napolitano, J.S. and Aprille, J.R., 2001, "Delocalized lipophilic cations selectively target the mitochondria of carcinoma cells," Adv. Drug Deliv. Rev., 49:63-701.		
/L.C./	65	National Institute of Health Consensus Development Conference Statement, 2001, "Adjuvant Therapy for Breast Cancer, November 1-3, 2000," J. Natl. Cancer Inst., 93:979-989.		
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/L.C./	67	Nicotera, P. and Leist, M., 1997, "Mitochondrial signals and energy requirement in cell death," Cell Death Differ., 4:516.		
/L.C./	68	Nobori, T., Karras, J.G., Della Ragione, F., Waltz, T.Z., Chen P.P. and Carson, D.A., 1991, "Absence of methylthioadenosine phosphorylase in human gliomas," Cancer Res., 51:3193-3197.		
/L.C./	69	Nobori, T., Szinai, I., Amox, D., Parker, B., Olopade, O.I., Buchhagen, D.L. and Carson, D.A., 1993, "Methylthioadenosine phosphorylase deficiency in human non-small cell lung cancers," Cancer Res., 53:1098-1101.		
/L.C./	70	Presta, M., Rusunati, M., Belleri, M., Morbedelli, L., Ziche, M. and Ribatti, D., 1999, "Purine analogue 6-methylmercaptopurine riboside inhibits early and late phases of the angiogenesis process," Cancer Res., 59:2417-2424.		
/L.C./	71	Raffray, M. and Cohen, G.M., 1997, "Apoptosis and necrosis in toxicology: a continuum or distinct modes of cell death?" Pharmacol. Ther., 75:153-177.		
/L.C./	72	Reed, J.C., 1995, "Regulation of apoptosis by bcl-2 family proteins and its role in cancer and drug resistance," Curr. Opin. Oncol., 7:541-546.		

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/L.C./	73	Roy, N., Dveraux, Q.L., Takahashi, R., Salvesen, G.S. and Reed, J.C., 1997, "The c-IAP-1 and c-IAP-2 proteins are direct inhibitors of specific caspases," <i>EMBO J.</i> , 16:6914-6925.		
/L.C./	74	Sausville, E.A. and Feigal, E., 1999, "Evolving approaches to cancer drug discovery and development at the National Cancer Institute," <i>USA Ann. Oncol.</i> , 10:1287-1291.		
/L.C./	75	Schmitt, C.A. and Lowe, S.W., 2002, "A senescence program controlled by p53 and p16 ink4a contributed to the outcome of cancer therapy," <i>Cell</i> , 109:335-346.		
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		Art Unit	1623
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/L.C./	83	Staunton, M.J. and Gaffney, E.F., 1998, "Apoptosis: basic concepts and potential significance in human cancer," Arch. Pathol. Lab. Med., 122:310-319.		
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/L.C./	85	Stolfi, R.L., Stolfi, L.M., Sawyer, R.C., and Martin, D.S., 1988, "Chemotherapeutic evaluation using clinical criteria in spontaneous, autochthonous murine breast tumors," J. Nat. Cancer Inst., 80:52-5.		
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/L.C./	94	Wielinga, P.R., Reid, G., Challa, E.E., van der Heijden, I., van Deemter, L., De Haas, M., Mol, C., Kuil, A.J., Groeneveld, E., Schuetz, J.D., Brouwer, C., De Abreu, R.A., Wijnholds, J., Beijnen, J.H. and Borst, P., 2002, "Thiopurine metabolism and identification of the Thiopurine metabolites transported by MRP4 and MRP5 overexpressed in human embryonic kidney cells," <i>Mol. Pharm.</i> , 62:1321-1331.	
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/L.C./	96	Woods, R.A., Henderson, R.M., and Henderson, J.F., 1978, "Consequences of inhibition of purine biosynthesis de novo by 6-methylmercaptopurine ribonucleoside in cultured lymphoma L5178 cells," <i>Euro. J. Cancer</i> , 14:765-70.	
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/L.C./	100	Young, I., Young, G.L., Wiley, J.S. and van der Weyden, M.B., 1985, "Nucleoside transport and cytosine arabinoside (ara C) metabolism in human T lymphoblasts resistant to ara C, thymidine and 6-methyemercap to purine riboside," <i>Eur. J. Cancer Clin. Oncol.</i> , 21(9):1077-1082.	
/L.C./	101	Zamzami, N., Susin, S.A., Marchetti, P., Hirsch, T., Gomez-Monterrey, I., Castedo, M., and Kroemer, G., 1996, "Mitochondrial control of nuclear apoptosis (see co-ents)," <i>J. Exp. Med.</i> , 183:1533-44.	
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/L.C./	103	European Communication for SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH, European Application No. 01986104.6 (Atty. Dkt. #636-A-PCT-EPO), Filed July 2, 2003, Dated September 6, 2007.	
/L.C./	104	U.S. Office Action for MARTIN et al., U.S. Serial No. 10/172,346 (Atty. Dkt. #636-B), Filed June 13, 2002, Dated November 19, 2003.	
/L.C./	105	U.S. Office Action for MARTIN et al., U.S. Serial No. 10/172,346 (Atty. Dkt. #636-B), Filed June 13, 2002, Dated June 15, 2005.	
/L.C./	106	U.S. Office Action for MARTIN et al., U.S. Serial No. 10/172,346 (Atty. Dkt. #636-B), Filed June 13, 2002, Dated June 15, 2006.	
/L.C./	107	Notice of Allowance and Fee(s) Due and Notice of Allowability, for MARTIN et al., U.S. Serial No. 10/172,346 (Atty. Dkt. #636-B), Filed June 13, 2002, Dated August 20, 2007.	
/L.C./	108	NIH R01 Grant Information for 1R01CA098505—1A3, PI Jason Koutcher, Project Title "Cytocidal Therapy In Vivo for Drug-Resistant Tumors," previously submitted for U.S. Serial No. 10/172,346 (Atty. Dkt. #636-B).	
/L.C./	109	National Cancer Institute RAID Grant Information, PI Maiyer Rizvi, previously submitted for U.S. Serial No. 10/172,346 (Atty. Dkt. #636-B).	

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